

1. A pharmaceutical dosage form which comprises a plurality of core particles, each core particle containing a drug; said particle being coated with:

- a) a first membrane of an enteric polymer;
- b) a second membrane of a combination of a water-insoluble polymer and an enteric polymer; and
- c) an intermediate membrane comprising an organic acid between the first and second membranes,

wherein said water-insoluble and said enteric polymers are present in said second membrane at a weight ratio of about 10:1 to 1:1,

the total weight of the first and second coatings is about 15 to 80 wt.% based on the total weight of the coated particles; and

wherein the first and second membranes can be coated on the core particle in either order.

2. A pharmaceutical dosage form as defined in claim 1 wherein said intermediate membrane further comprises a polymeric binder.

3. A pharmaceutical dosage form as defined in claim 1 wherein the intermediate membrane is about 5% to about 20% of the total weight of the coated particles.

4. A pharmaceutical dosage form as defined in claim 1 wherein the aqueous solubility of said drug varies from about 0.1 mg/mL to about 1,000 mg/mL.

5. A pharmaceutical dosage form as defined in claim 1 wherein the drug substance is selected from the group consisting of analgesics, anticonvulsants, anesthetics, antidiabetic agents, anti-infective agents, antineoplastics, antiParkinsonian agents, antirheumatic agents, cardiovascular agents, central nervous system (CNS) stimulants, dopamine

receptor agonists, gastrointestinal agents, psychotherapeutic agents, urinary tract agents or combinations thereof.

6. A pharmaceutical dosage form as defined in claim 1 wherein the drug substance is selected from the group consisting of albuterol sulfate, amoxicillin, bupropion hydrochloride, carbidopa, cefaclor, diclofenac sodium, erythromycin, felodipine, loratidine, lithium carbonate, methylphenidate, metoprolol tartrate, nifedipine, omeprazole, sotalol hydrochloride, verapamil hydrochloride and combinations thereof.

7. A pharmaceutical dosage form as defined in claim 1 wherein the core particle is a non-pareil sugar seed coated with a drug and polymeric binder or the core particle is a particle prepared by granulation and milling or by extrusion/spheronization to form an active drug particle.

8. A pharmaceutical dosage form as defined in claim 1 wherein said enteric polymer is selected from the group consisting of esters of cellulose, polyvinyl acetate phthalate, pH sensitive methacrylic-methylmethacrylate copolymers and shellac.

9. A pharmaceutical dosage form as defined in claim 1 wherein said water insoluble polymer of the second coating is selected from the group consisting of ethylcellulose, polyvinyl acetate, neutral copolymers based on ethyl acrylate and methylmethacrylate and copolymers of acrylic and methacrylic acid esters having quaternary ammonium groups.

10. A pharmaceutical dosage form as defined in claim 1 wherein at least one of said membranes further comprises a plasticizer.

11. A pharmaceutical dosage form as defined in claim 10 wherein said plasticizer is selected from the group consisting of triacetin, tri-butyl citrate, tri-ethyl citrate, acetyl tri-n-butyl citrate, diethyl phthalate, castor oil, dibutyl sebacate, acetylated monoglycerides and mixtures thereof.
12. A pharmaceutical dosage form as defined in claim 1 wherein said membrane coating is applied from a solution in a pharmaceutically acceptable solvent or from an aqueous dispersion of the enteric polymer, water insoluble polymers or their mixtures.
13. A pharmaceutical dosage form as defined in claim 1 wherein said second coating of a mixture of water insoluble and enteric polymers is applied to a thickness of from about 35% to about 55% based on the total weight of the dosage form.
14. A pharmaceutical dosage form as defined in claim 1 wherein said organic acid of the intermediate membrane applied between the first and second membranes is selected from the group consisting of fumaric acid, succinic acid, tartaric acid, citric acid, malic acid, maleic acid and combinations thereof.
15. A pharmaceutical dosage form as defined in claim 1 wherein said pharmaceutical dosage form is in the form of a hard gelatin capsule.
16. A pharmaceutical dosage form as defined in claim 15 wherein said capsule comprises a single form of the particle to provide a time-controlled pulsatile release of the drug three to six hours upon oral administration.
17. A pharmaceutical dosage form as defined in claim 15 wherein said capsule comprises a single form of the particle to provide a time-controlled pulsatile release of the drug at or near a patient's duodenum/jejunum or colon.

18. A pharmaceutical dosage form as defined in claim 15 wherein said capsule comprises two or more populations of multicoated drug particles wherein each population exhibits different release characteristics.
19. A pharmaceutical dosage form as defined in claim 15 wherein said capsule contains multicoated particles of two or more drugs.
20. A method of making a drug delivery system which comprises:
- a) preparing a core particle comprising a drug;
  - b) coating said drug-containing core particle with a plasticized enteric polymer membrane;
  - c) coating said plasticized enteric coated drug particle with an intermediate membrane containing an organic acid; and
  - d) coating the intermediate membrane with a membrane comprising a mixture of a water insoluble polymer and enteric polymer wherein said water insoluble polymer and said enteric polymer are present at a weight ratio of from about 10:1 to 1:1;
- wherein the total weight of the coatings is about 15 to 80 weight percent based on the total weight of the coated particles.